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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/257,650	02/25/99	FUJINO	M 48194

HM12/0124

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EXAMINER	
O HARA,E	
ART UNIT	**PAPER NUMBER**
1646	12

DATE MAILED: 01/24/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/257,650	Masahiko
Examiner	**Group Art Unit**
Eileen B. O'Hara	1646

☒ Responsive to communication(s) filed on *Nov. 17, 1999*

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *1-26* is/are pending in the applicat

Of the above, claim(s) *1-13* is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *14-26* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☒ Claims *1-26* are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☒ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☒ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *6 and 7*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. Claims 1-26 are pending in the instant application.

Applicant's election without traverse of Group V, claims 14-26 in Paper No. 10 is acknowledged.

Claims 1-13 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b) as being drawn to a non-elected invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 14-26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of screening for a substance that restores normal function to a known receptor with a mutation, does not reasonably provide enablement for a method of screening for a substance that restores normal function to any mutant gene product. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

These claims encompass a method of screening for substances that compensate for or restore normal function to a gene product, which may be a receptor, which has a mutation that results in inactivity or altered activity and results in disease, and which may be a natural ligand. Methods of screening for substances that affect the activity of receptors are old and well known in the art, and it is well known that receptors with decreased binding affinity for their ligands can be activated at wild-type or close to wild-type levels by supplying higher levels of the natural ligand. For example Ullrich et al. (PN 5,861,266) discloses that insulin resistance can be due to insufficient insulin receptor expression or reduced insulin binding affinity, both of which can be caused by a mutation in the structural gene for the insulin receptor, and patients with diabetes can be treated with insulin (column 3, lines 10-48).

However, because these claims encompass any gene product having a mutation and altered activity, and the specification does not disclose a single working embodiment of a specific gene product or receptor, a disease or disorder associated with a gene product having a mutation, or possible substances that would restore activity to such gene products or compensate for the mutant gene product activity, the claims are not enabled. The methods claimed do not distinguish between compensating for mutant gene product activity, as in Ullrich, or restoring wild-type activity to a mutant gene product, which would be highly unpredictable. The instant specification does not provide a method through which an artisan can determine if a substance restores wild-type activity to a mutant gene product, because the instant specification does not disclose any specific function of any product.

Due to the large quantity of experimentation necessary to determine if a substance of any kind restores activity to any aberrant gene product, the lack of direction/guidance presented in the specification regarding same, the absence of working examples directed to same, the complex nature of the invention, and the breadth of the claims which fail to recite particular biological activities, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope. What Applicant has provided is a mere wish or plan and an invitation to experiment.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 14-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

3.1 The claims are generally narrative and indefinite, failing to conform with current U.S. practice. They appear to be a literal translation into English from a foreign document and are replete with grammatical and idiomatic errors.

3.2 Claims 14, 24 and dependent claims 15, 25 and 26 are vague and indefinite because they recite the term "operating an aberrant gene product", and it is not clear how the substance "operates" the gene product.

3.3 Claim 14 and dependent claim 15 are indefinite because claim 14 recites the term "subject substance" and is not clear what this term means.

3.4 Claims 14, 16, 20, 21 26 and dependent claims 15, 18, 19, 22, 23 and 25 are also vague and indefinite for reciting the terms "assaying the operation activity", "operate the signal transduction system" and "normally operates said product". Again it is not clear what "operating" means in the context of the claims.

3.5 Claim 16 and dependent claims 18 and 19 are indefinite because claim 16 recites the limitation "**The** screening method" , and there is insufficient antecedent basis for this limitation in the claim.

3.6 Claim 16 and dependent claims 18 and 19 are indefinite because the word "**and**" on the third line of claim 16 should be "**with**".

3.7 Claims 18 and 19 are indefinite because they recite the limitation "the aberrant **receptor**" and there is no sufficient antecedent basis for this limitation in the claim.

3.8 Claims 18, 22 and dependent claims 19 and 23 are indefinite because claims 18 and 22 recite the term "an aberrant receptor **prepared** by expressing in a cell". In order to prepare a receptor, there must be steps to isolate the receptor after expression in a cell, and no such steps are recited in the claim, so that it is incomplete.

3.9 Claims 19 and 23 are indefinite because it is not clear how the gene is "specified", or what that means.

3.10 Claims 20, 21 and dependent claims 22 and 23 are indefinite because the first lines of claims 20 and 21 encompass a method of preparing a drug for treatment of a disease, but what follows is a method for a screening assay, not a method for preparing a drug.

3.11 Claim 24 is indefinite because it is not clear what "separating the aberrant gene product" means, because there is no recitation of what it is being separated from.

3.12 Claim 24 is also indefinite because in the sections "providing a substance **as** the aberrant gene product" and "determining operation activity of said substance **as** said gene product", the implication is that the substance to be screened **is** the aberrant gene product.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> > (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 14-25 are rejected under 35 U.S.C. 102(b) as being anticipated by Lebrun et al., The Journal of Biological Chemistry, Vol. 268, No. 15, pages 11272-11277, May 25, 1993.

Claims 14-25 encompass a method of screening for a substance capable of restoring activity to a mutant gene product which may be a receptor, by bringing the substance into contact with the receptor and assaying the receptor activity, in which the mutant receptor is expressed in

a cell, causes a disease in a mammal, is compared to activity of wild type gene product, and in which the mutant gene product is purified.

Lebrun et al. disclose a naturally occurring mutation in the insulin receptor (aberrant gene product) isolated from two sisters, which causes the disease of extreme insulin resistance. This receptor mutation impairs the ability of the hormone to activate autophosphorylation of receptors and phosphorylation of substrates (operation activity). Lebrun et al. teach a method of screening for monoclonal antibodies (substance or drug) that restores activity (operation activity) to the mutant receptor by assaying the activity of the receptor. An activity assayed was phosphorylation of substrate (signal transduction system), the screen was performed in NIH 3T3 fibroblasts transfected with the gene encoding and expressing either the wild-type or mutant receptors, assays were performed on purified receptors (separating the aberrant gene product), and the activity of the mutant receptor was compared to that of the wild-type receptor. Two monoclonal antibodies were found to activate the mutant receptor kinase.

Conclusion

5. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eileen B. O'Hara, whose telephone number is (703) 308-3312. The examiner can normally be reached on Monday through Friday from 9:00 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached at (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Eileen B. O'Hara, Ph.D

Patent Examiner

LORRAINE SPECTOR
PRIMARY EXAMINER